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FREE 17-HYDROXYCORTICOSTEROID LEVELS IN PAROTID FLUID, SERUM, A--ETC(U)
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School of Aviation Medicine
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FREE 17-HYDROXYCORTICOSTEROID LEVELS IN PAROTID FLUID, SERUM, AND URINE FOLLOWING THE ORAL ADMINISTRATION OF SYNTHETIC ANALOGS OF HYDROCORTISONE

In a study of free 17-hydroxycorticosteroids, measurable levels were consistently found in human parotid fluid. Under the influence of synthetic adrenocortical analogs, altered parotid steroid levels closely paralleled changes evidenced in serum and urine 17-OHCS concentration. These findings suggest that steroid values in parotid fluid can be used as an indicator of adrenocortical status.

Measurement of the concentration of adrenocortical steroids, or their degradation products, in body fluids provides a sensitive approach to the study of adrenal cortical function. Thus, reliance is placed upon such findings in hypo- and hyper- disease states of the cortex as well as in endogenous hyperactivity states resulting from stress.

Studies of adrenocortical steroid concentration have been confined mainly to blood and urine. This paper describes results obtained from the analysis of human parotid fluid and serum for free (nonconjugated) 17-hydroxycorticosteroids (17-OHCS), and urine for total 17-OHCS, before and after the oral administration of synthetic adrenocortical analogs. These drugs serve to alter serum and urine corticoid levels, in order to ascertain whether the concentration of 17-OHCS in parotid fluid would undergo concomitant changes.

The subjects were healthy males between 17 and 22 years of age, who had recently been found physically qualified for military service. Environmental exposure was virtually identical for all subjects, as were meal times, types of food ingested, and times of arising and retiring. Blood was collected by venipuncture, and the serum retained. A plastic vacuum cup was used to collect the parotid fluid, which was stimulated by the chewing of 3.0 gm. of sugared gum; a clearance sample was collected prior to each test collection. Parotid fluid and blood samples were collected immediately prior to the oral administration of 50 mg. of the drug under study, and subsequent collections of both fluids were made at 2, 4, and 6 hours after dosage. Urine voided during the 6-hour period was collected. No food was allowed from 3 hours prior to drug administration until completion of the experiment.

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The concentration of free 17-OHCS in parotid fluid and in serum was determined by the method of Peterson et al. (1), utilizing a methylene chloride extraction procedure. Total 17-OHCS levels in urine were analyzed by the butanol extraction method of Reddy (2). Both technics employ the Porter-Silber (3) color reaction between 17, 21-dihydroxy-20-ketosteroids and phenylhydrazine.

Four experimental groups were studied. Each group included 8 subjects who were given a 50-mg. drug dose orally and 4 who participated as untreated controls. A total of 16 control subjects was studied and the results grouped for the final control baselines. The drugs employed were hydrocortisone, prednisolone (delta-1 hydrocortisone), medrol (delta-1, 6-methyl hydrocortisone), and triamcinolone (delta-1, 9-alpha-fluoro, 16-hydroxy hydrocortisone).

Prednisolone, hydrocortisone, and medrol gave marked increases in free 17-OHCS appearing in serum (fig. 1). Prednisolone prompted the greatest rise, with a peak level about 4.5 times that of pre-drug levels. All three drug groups peaked at the 2-hour sampling time.

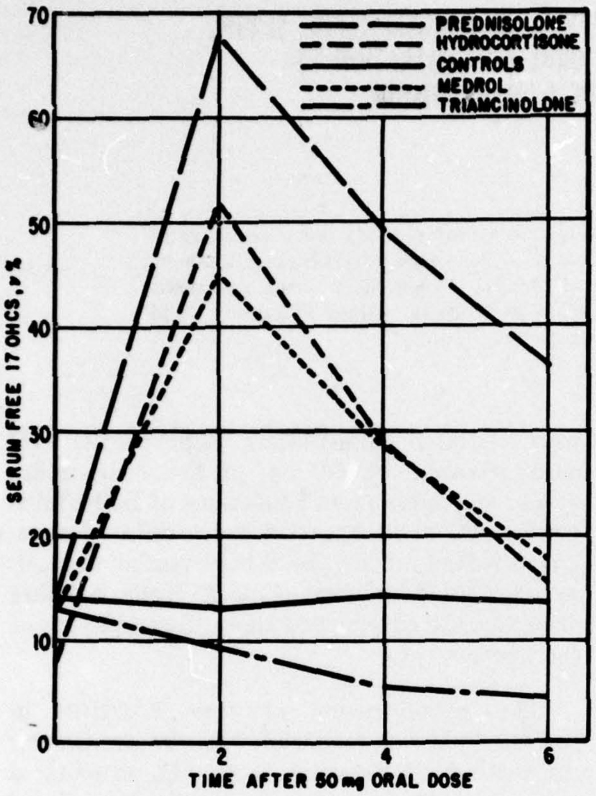

FIGURE 1

Free 17-hydroxycorticosteroid levels in serum following oral administration of synthetic analogs of hydrocortisone.

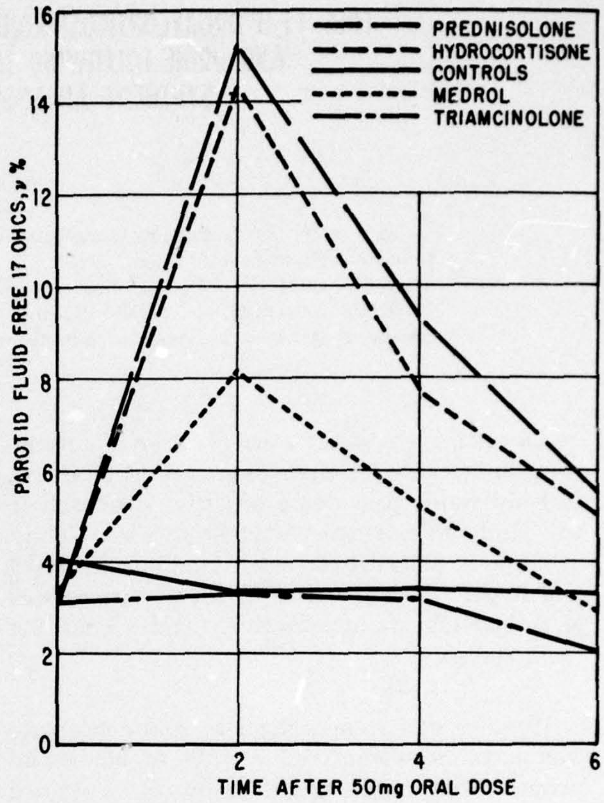

FIGURE 2

Free 17-hydroxycorticosteroid levels in parotid fluid following oral administration of synthetic analogs of hydrocortisone.

Control subjects demonstrated no change in levels with the passage of time, while triamcinolone produced a decrease in serum 17-OHCS levels. As shown in figure 2, free 17-OHCS levels observed in parotid fluid closely paralleled the serum findings. Prednisolone, hydrocortisone, and medrol have marked increases in levels, the rise following prednisolone being approximately fivefold. Again, triamcinolone led to a depression of free steroid levels.

The decreased concentration associated with triamcinolone dosage was due to the fact that this preparation, unlike the other drugs under study, does not give a Porter-Silber color reaction. Although it has the basic structure said to be necessary for the reaction (17, 21-dihydroxy-20-ketosteroid), this drug, when dissolved in slightly acid water, gives a negative Porter-Silber response. The OH group at C-16 is definitely implicated since the methyl group at C-16 in decadron (delta-1, 9-alpha-fluoro, 16-methyl hydrocortisone) does not interfere with the color reaction. Thus, it becomes apparent that triamcinolone, since it is not determinable by the phenylhydrazine reaction, produces a drop in measurable 17-OHCS by suppression of endogenous adrenocortical secretion.

The urinary excretion of total 17-OHCS (free plus conjugated), prompted by prednisolone, averaged 1.85 mg./hr. over the 6-hour sampling period; this exceeded the 0.40 mg./hr.

excretion in untreated controls. As with serum and parotid fluid, marked increases also followed medrol and hydrocortisone dosage, 17-OHCS excretion values averaging 1.47 mg./hr. and 1.27 mg./hr., respectively. The urine 17-OHCS concentration following triamcinolone was less than that in the control subjects (0.38 mg./hr. compared to the control excretion of 0.40 mg./hr.), but was not depressed as much as the equivalent level in serum and parotid fluid. This would suggest an effect on conjugated forms, while free 17-OHCS alone is measured in serum and parotid fluid.

These findings suggest that steroid values in parotid fluid can be used as an indicator of adrenocortical status. This method does not present the problems encountered with multiple blood sampling. Continuous parotid sampling is possible since the parotid cap may be left in place for an extended period. Sampling periods up to 3 hours' continuous stimulation showed no diminution in parotid fluid 17-OHCS concentration. Further, the steroid concentration is apparently independent of parotid flow rates. While comparable steroid levels can be found in whole saliva, parotid sampling is more desirable for the following reasons: pipetting is more precise; bacterial contamination is less likely to occur; the sample is likely to contain less sloughed tissue; and it can be more easily stored.

Studies utilizing parotid fluid 17-OHCS levels are of particular value to those investigators who require a sampling method that is completely devoid of stress-producing factors and is adaptable for use in such very restricted operating quarters as those of hypersonic fighter aircraft and space-flight simulators.

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